EXERCISE RESPONSES ASSOCIATED WITH ALTITUDE ACCLIMATIZATION ARE RETAINED DURING REINTRODUCTION TO 4,300 M

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Running Head: Reintroduction to altitude

ABSTRACT

Following 2-3 wk of altitude acclimatization, ventilation is increased and heart rate (HR), plasma volume (PV) and lactate accumulation ([La]) are decreased during submaximal exercise. We hypothesized that some degree of exercise responses associated with acclimatization would be retained upon reintroduction to altitude (RA) after 8 d at sea level (SL). Six male lowlanders exercised to exhaustion (EXH) at the same relative percentages of peak oxygen uptake at SL, on acute altitude (AA) exposure, after a 16-d chronic altitude (CA) exposure on Pikes Peak (4,300 m), and during a 3-4-h RA after 8 d at SL. The EXH time was the same at SL (66.0±1.6 min), AA (67.7±7.3 min), CA (79.9±6.2 min) and RA (67.9±1.9 min). At 75% $\dot{V}O_{2peak}$: (1) arterial oxygen saturation (SaO_2) increased from AA to CA (67.0±1.5 vs. 78.5±1.8%; $P<0.05$) and remained increased at RA (77.0±2.0%); (2) HR decreased from SL to CA (171±6 vs. 152±9 bpm; $P<0.05$) and remained decreased at RA (157±5 bpm); (3) calculated PV decreased 6.9±10.0% at AA, 21.3±11.1% at CA, and 16.7±5.4% at RA from SL baseline values, and (4) [La] decreased from AA to CA (5.1±0.9 vs. 1.9±0.4 $mmol \cdot l^{-1}$; $P<0.05$) and remained decreased at RA (2.6±0.6 $mmol \cdot l^{-1}$). For each individual, percent retention of acclimatization response was calculated as (RA-AA)/(CA-AA)*100. Upon RA after 8 d at SL, the acclimatization responses were retained 92±9%for SaO_2, 74±8% for PV, and 58±3% for [La] at 75% $\dot{V}O_{2peak}$. Although exhaustion time is not improved upon reintroduction to altitude after eight days at sea level, retention of beneficial exercise responses associated with altitude acclimatization is likely in individuals whose work, athletic competition, or recreation schedules involve intermittent sojourns to high elevations.

Key words: lactate, ventilation, heart rate, plasma volume, altitude deacclimatization

IINTRODUCTION

Acclimatization to altitude is a process, occurring over a 2-3 wk period, that results in systemic adaptations that can be measured as physiological responses. Some of these physiological responses include an increase in ventilation ($\dot{V}_E$) (15), a decrease in heart rate (HR) (34), plasma volume (PV) (23), and blood lactate accumulation ([La]) during submaximal exercise (35) relative to initial altitude exposure. These responses may contribute to the dramatically improved submaximal exercise capacity observed in the well-acclimatized lowlander (18,26). The time course for each of these responses is variable. Some are fully manifest within days of arriving at altitude while others require 2-3 wk (36). Although the time course for altitude acclimatization has been well studied, the time course for deacclimatization to altitude, that results in the loss of systemic adaptations and measured physiological responses associated with acclimatization, has received little attention.

Studies examining deacclimatization to altitude have generally performed post-exposure measurements only at low altitude. These investigations reported that physiological responses expressed with acclimatization to altitude persist for d to wk after returning to low altitude (14,22,23,32). Both Sato et al. (32) and Forster et al. (12) reported an increased resting ventilatory response to hypoxia compared to pre-exposure responses from as few as 4 d to as long as 45 d after return to low altitude. In mountaineers, the decrease in resting HR after acclimatization to 4,000 m persisted for at least 13 d after returning to low altitude (22). Krzywicki et al. (23) reported that the decrease in PV that was apparent 4 d into a 12-d acclimatization to 4,300 m returned to pre-acclimatization values after a 4-d return to low altitude. The decrease in peak [La] that was apparent after 3 wk of a 5-wk acclimatization to

5,200 m persisted for 3 wk following a return to low altitude (14). These studies suggest that some degree of altitude acclimatization, measured at low altitude, is retained after a period of time at low altitude. However, since post-exposure measurements were not made at high altitude, we do not know whether some degree of altitude acclimatization is retained during a reintroduction to altitude.

Koller et al. (22) did make post-exposure measurements at rest during a 2-hr stepwise RA in acclimatized mountaineers and non-acclimatized males. They reported a significantly higher $\dot{V}_E$ and lower HR during RA in mountaineers than in non-acclimatized males after a 13-35 d low altitude deacclimatization. The problem with this study is that neither pre-exposure nor chronic-exposure measurements were made. Therefore, whether the mountaineers had different physiological responses from the non-acclimatized males before beginning their expedition remains unknown. Furthermore, we do not know if their physiological responses changed with acclimatization to altitude. The data from this study suggest but do not prove that resting ventilatory and cardiovascular responses to acclimatization were retained during RA after a period of time at low altitude.

Retention of altitude acclimatization during RA is likely given that retention of acclimatization, measured at low altitude, occurs after a period of residence at low altitude. However, the magnitude of physiological responses measured during exercise during RA may be different due to the added stimulation of hypoxia and exercise. Preservation of some of the physiological responses associated with altitude acclimatization during RA, such as those that dramatically improve submaximal exercise performance, have important implications for people whose work, athletic competition, or recreation schedules involve intermittent sojourns to high

elevations. The purpose of this study was to test the hypothesis that some degree of exercise responses associated with altitude acclimatization would be retained upon RA after 8 d at sea level (SL).

METHODS

Volunteer test subjects. Six male volunteers participated in this study. They had a mean (±SE) age, initial body weight (BW), height, and percent body fat, determined by hydrostatic underwater weighing, of 31±2 yr, 82.4±4.6 kg, 180±10 cm, and 16.5±1.6%, respectively. These men were randomly selected as a subset from 12 volunteers who participated in a larger study on acclimatization and deacclimatization to altitude. Each was a lifelong, low-altitude resident and had no exposure to altitudes greater than 1,000 m for at least 6 mo prior to the study. All were healthy, physically active members of a U.S. Army Special Forces unit. Each provided written acknowledgment of his informed consent and was made aware of his right to withdraw without prejudice at any time.

Study protocol. This study used a repeated measures design in which each volunteer served as his own control. The study consisted of four phases: a) a 10-d SL phase at Natick, MA (50 m); b) a simulated acute altitude (AA) exposure (<2 h) phase in a hypobaric chamber (4,300 m, 446 mm Hg); c) an 18-d chronic altitude (CA) phase on the summit of Pikes Peak, CO (4,300 m); and d) a 3-4 h RA phase in a hypobaric chamber (4,300 m, 446 mm Hg) after 8 d at SL. Volunteers were transported to and from Pikes Peak by commercial plane and automobile in approximately 8 h. After the volunteers entered the hypobaric chamber for the AA and RA phases, the chamber was decompressed to the barometric equivalent of 4,300 m over a period of approximately 12 min. All exercise tests in the hypobaric chamber were initiated within 30 min

of arriving at 4,300 m. During exercise testing sessions, temperature and relative humidity were maintained at 21±2°C and 50±5%, respectively. The volunteers had unrestricted access to fluid and food throughout the study.

Exercise testing. All volunteers completed a submaximal exercise to exhaustion (EXH) test at SL, AA, CA, and RA and a peak oxygen uptake ($\dot{V}O_{2peak}$) test at SL, AA, and CA. A fourth $\dot{V}O_{2peak}$ test was not conducted during RA based on previous reports showing that $\dot{V}O_{2peak}$ does not change from AA to RA after 5 d at SL (7). The $\dot{V}O_{2peak}$ and EXH tests were separated by at least 48 h. For the CA phase, the $\dot{V}O_{2peak}$ and EXH tests were performed on days 14 and 16 at 4,300 m, respectively. All exercise testing was performed at the same time of day for each volunteer. Prior to all exercise tests, the volunteers were required to abstain from alcohol for at least 48 h and not exercise on the actual day of testing. Otherwise, volunteers maintained the same level of physical activity throughout the study.

For each exercise testing session, the volunteer was weighed (T-shirts, shorts, and socks) to the nearest 0.1 kg, and electrocardiogram (EKG) electrodes were attached. During exercise, HR was determined from continuous EKG recordings (Cardiovit AT-6C; Schiller Canada, Inc., Nepean, Ontario). Respiratory gas measurements were made continuously by open-circuit calorimetry using an appropriately calibrated metabolic cart (Model 2900; SensorMedics Corporation, Anaheim, CA), which provided values for oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), respiratory exchange ratio (RER), and minute ventilation ($\dot{V}E$). Arterial oxygen saturation (SaO_2) was measured by finger pulse oximetry (Oxyshuttle; SensorMedics Corporation, Anaheim, CA). Cardiorespiratory measurements were made while the volunteer stood at rest before the exercise test began and again during exercise testing (See below). The

ventilatory equivalent for CO_2 ($\dot{V}E \cdot \dot{V}CO_2^{-1}$) was calculated from individual $\dot{V}E$ and $\dot{V}CO_2$ data in order to minimize intra-subject variability in $\dot{V}E$ due to different body sizes and metabolic rates.

For each individual, percent retention of acclimatization-associated response for each variable was calculated as the difference in the CA response from the AA response divided by the difference between the RA response from the AA response, i.e. (RA-AA)/(CA-AA)*100. The fractional contribution of fat and carbohydrate to energy expenditure during exercise testing was calculated using the tables of Lusk (24).

Peak exercise testing. The $\dot{V}O_{2peak}$ was determined by a progressive-intensity, continuous treadmill running test to exhaustion described by Sawka et al. (33). The volunteers performed a warm-up bout of 10 min walking (1.56 $m \cdot s^{-1}$) at a 10% treadmill grade. At SL, if a volunteer's HR exceeded 140 bpm during warm-up, the treadmill speed was set at 2.68 $m \cdot s^{-1}$; if HR was ≤ 140 bpm, the speed was set at 3.13 $m \cdot s^{-1}$. The initial incline was 5% followed by 2.5% increments every 1.5 min for all volunteers. Based on the ~33% expected reduction in $\dot{V}O_{2peak}$ at altitude (21), volunteers ran at 2.68 $m \cdot s^{-1}$ at AA, CA, and RA. The highest oxygen uptake achieved for one min was recorded as $\dot{V}O_{2peak}$. After the $\dot{V}O_{2peak}$ test, a 4-min post-exercise blood sample was drawn by venipuncture for evaluation of blood [La] and glucose [GLU].

Submaximal exercise testing. Prior to the EXH test, a cannula was inserted into a superficial arm vein and kept patent with a dilute heparin solution to allow serial blood samples to be collected without repeat venipuncture. A 20-min equilibration period (standing) was completed prior to obtaining the 10-ml resting blood sample for evaluation of [La], [GLU],

hemoglobin [Hb], hematocrit (Hct), glycerol [GLY], cortisol [COR], and free fatty acids [FFA]. Additional blood samples were taken at 10, 40, and 60 min, and at exhaustion. Two ml of whole blood from each sample was immediately assayed for [La], [GLU], [Hb], and Hct. The remaining 8 ml of blood was centrifuged, and the plasma was aliquoted, frozen, and stored at -80°C until final analysis.

Each volunteer exercised at 40% of his altitude-specific $\dot{V}O_{2peak}$ for the first 15 min, 75% $\dot{V}O_{2peak}$ from 15 to 60 min, and 85% $\dot{V}O_{2peak}$ from 60 min to exhaustion. Treadmill speed and/or grade were adjusted to reach the desired percentage of $\dot{V}O_{2peak}$ for each volunteer. In all cases, the required percentage of $\dot{V}O_{2peak}$ was obtained within 10 min of the beginning of each stage. The $\dot{V}O_2$s for each stage of exercise during RA were maintained identically to those during the CA phase. Cardiorespiratory measurements were obtained during the last 10 min of each exercise stage, and the mean value collected during the last three min of the test was analyzed. The volunteers were aware of their ongoing exercise time during the submaximal exercise test. Volunteers refrained from consuming any nutrients for approximately the same number of hours before each EXH test.

Blood analyses. Aliquots of heparinized blood were analyzed for [La], [GLU], [Hb], and Hct. Blood [La] and [GLU] were measured in duplicate using a glucose/lactate analyzer (Model 2300; Yellow Springs Instruments, Yellow Springs, OH). The [Hb] was measured in duplicate using a hemoximeter (Radiometer, Inc., Copenhagen, Denmark). The Hct was measured in triplicate using heparinized microcapillary tubes. Changes in [Hb] and Hct from SL baseline values were used to calculate changes in PV (8). Plasma concentrations of [GLY] and [FFA] (Sigma Chemical Company, St. Louis, MO; Wako Chemicals USA, Inc., Richmond, VA)

were determined by enzymatic colorimetric assays in duplicate using a spectrophotometer (Model Lamda 3A; Perkin-Elmer Co., Norwalk, CT). Plasma concentrations of [COR] were determined in duplicate using a solid phase ^{125}I radioimmunoassay (Diagnostic Products Co., Los Angeles, CA) and a gamma counter (Model 5002; Packard Instrument Co., Meriden, CT). Blood [GLU] and plasma [GLY], [FFA], and [COR] were analyzed to determine differences in substrate utilization between the four study phases. The intraassay variances for [GLY], [FFA], and [COR] were 3.7%, 2.6%, and 4.5%, respectively. All samples for one volunteer were analyzed in the same assay to avoid interassay variations. All samples were thawed once for each assay procedure.

Statistical analyses. One way ANOVAs with repeated measures were used to analyze the differences between study phases for all data, except the blood parameters collected during the EXH test, which were analyzed using two-way ANOVAs (study phase, sample time) with repeated measures for both factors. Significant main effects and interactions were analyzed using Tukey's least significant difference test. Statistical significance was set at $P < 0.05$. All data are presented as means ± SE.

RESULTS

Peak exercise testing. Cardiorespiratory and metabolic responses collected during $\dot{V}O_{2peak}$ testing are presented in Table 1. The ~ 30% decrease in $\dot{V}O_{2peak}$ from SL to AA remained decreased at CA. The $[La]_{peak}$ did not change significantly from SL to AA, but decreased ~45% from AA to CA. As expected, SaO_{2peak} was decreased at AA and CA compared to SL values and tended to increase from AA to CA. Although not statistically significant, $\dot{V}E_{peak}$ tended to be higher at CA compared to SL and AA. The HR_{peak} decreased ~10% from SL

to CA, but there was no difference in HR_{peak} between SL and AA. The RER_{peak} did not change from SL to AA, but decreased ~12% at CA compared to both SL and AA values.

Submaximal exercise testing. The EXH time was the same at SL (66.0±1.6 min), AA (67.7±7.3 min), CA (79.9±6.2 min) and RA (67.9±1.9 min). The EXH time tended to increase (~16%) from AA to CA. The cardiorespiratory responses during the EXH test are presented in Figure 1. As expected, absolute $\dot{V}O_2$ was the same at AA, CA, and RA at all workloads, but was significantly higher at SL since volunteers were tested at their relative percentages of $\dot{V}O_{2peak}$. The SaO_2 decreased ~30% from SL to AA, but then increased ~15% from AA to CA and remained increased at RA at all workloads. The $\dot{V}E \cdot \dot{V}CO_2^{-1}$ increased ~40% at all workloads from SL to AA. At 40% $\dot{V}O_{2peak}$, $\dot{V}E \cdot \dot{V}CO_2^{-1}$ increased ~26% from AA to CA and remained increased at RA. At 75% $\dot{V}O_{2peak}$ and exhaustion, $\dot{V}E \cdot \dot{V}CO_2^{-1}$ tended to increase from AA to CA. There were no differences in HR from SL to AA, but HR decreased ~10% from SL to CA and remained depressed at RA at 75% $\dot{V}O_{2peak}$ and exhaustion.

The RER decreased from SL to CA at 40% $\dot{V}O_{2peak}$ (0.90±0.04 to 0.81±0.01; $P<0.05$), but not at 75% $\dot{V}O_{2peak}$ (0.94±0.01 to 0.90±0.01), and exhaustion (0.91±0.04 to 0.91±0.02). When compared to CA values, RER did not change at RA at 40% $\dot{V}O_{2peak}$ (0.81±0.03), 75% $\dot{V}O_{2peak}$ (0.89±0.02) and exhaustion (0.91±0.03). The fractional contribution of fat to total energy expenditure, calculated from $\dot{V}O_2$ and RER data, increased ($P<0.05$) from SL (32.0±6.0%) to CA (61.3±4.5%) and RA (61.0±10.0%) only at 40% $\dot{V}O_{2peak}$. However, the tendency for an increased fractional contribution of fat to total energy expenditure at 75% $\dot{V}O_{2peak}$ at CA (31.5±4.7%) and RA (36.9±5.1%) compared to SL (17.5±4.3%) was not significant.

The [La] data collected during the EXH test are presented in Figure 2. Blood parameters at min 40 and min 60 (both at 75% $\dot{V}O_{2peak}$) were not significantly different, therefore, the mean value of these two time periods was used to represent values at 75% $\dot{V}O_{2peak}$. The [La] at 75% $\dot{V}O_{2peak}$ was ~63% lower at CA (1.9±0.3 mmol·l^{-1}) compared to AA (5.1±0.6 mmol·l^{-1}). The [La] at exhaustion also decreased ~50% from AA (6.6±0.9 mmol·l^{-1}) to CA (3.3±0.4 mmol·l^{-1}). At RA compared to CA, [La] was similar at both 75% $\dot{V}O_{2peak}$ (2.6±0.4 mmol·l^{-1}) and exhaustion (3.3±0.6 mmol·l^{-1}).

The [GLU], [GLY], [FFA], and [COR] data collected during the EXH test were not significantly different between study phases. Blood [GLU] ranged from rest to exhaustion, respectively, 76-109 μg·dl^{-1} at SL, 85-117 μg·dl^{-1} at AA, 73-115 μg·dl^{-1} at CA, and 84-103 μg·dl^{-1} at RA. [GLY] ranged from 0.18-0.30 mmol·l^{-1} at SL, 0.19-0.39 mmol·l^{-1} at AA, 0.23-0.44 mmol·l^{-1} at CA, and 0.27-0.51 mmol·l^{-1} at RA. [FFA] ranged from 0.37-0.60 mmol·l^{-1} at SL, 0.26-0.61 mmol·l^{-1} at AA, 0.28-0.62 mmol·l^{-1} at CA, and 0.37-0.86 mmol·l^{-1} at RA. [COR] ranged from 16.4-21.4 μg·dl^{-1} at SL, 12.3-17.9 μg·dl^{-1} at AA, 16.1-21.1 μg·dl^{-1} at CA, and 15.1-21.6 μg·dl^{-1} at RA. All of these accumulation values tended to increase with exercise time, but significant main effects of time are not reported.

The [Hb] and Hct did not change from rest to exhaustion during the EXH test in all study phases. Both [Hb] and Hct (mean of the four time periods) were increased ($P<0.05$) at CA (17.1±0.7 g·dl^{-1}; 46.9±2.0%) compared to SL (15.1±0.3 g·dl^{-1}; 39.1±0.7%) and AA (15.5±0.3 g·dl^{-1}; 41.3±1.2%) and remained elevated at RA (16.1±0.5 g·dl^{-1};45.1±1.2%). Calculated PV decreased 6.0±3.5% at AA, 22.3±4.5% at CA, and 15.4±2.4% at RA from SL baseline values. The BW did not change from SL (82.4±4.6 kg) to AA (82.1±4.5 kg) and decreased ($P<0.05$)

from AA to CA (80.5±4.5 kg). BW rebounded at RA to 82.0±3.9 kg, which was similar to values at SL and AA. Figure 3 shows the percent retention of acclimatization-associated responses upon RA after 8 d at SL in variables that showed a significant acclimatization response from AA.

DISCUSSION

To determine whether exercise responses associated with altitude acclimatization were retained upon RA after 8 d at SL, it was necessary first to examine whether appropriate acclimatization responses were exhibited. Significant increases in peak and submaximal exercise SaO_2 and $\dot{V}E \cdot \dot{V}CO_2^{-1}$ confirmed the presence of ventilatory acclimatization. The magnitude of the ventilatory adaptations observed in our study were comparable to those reported by others studying well-acclimatized males at 4,300 m (4,28). The significant decrease in HR from SL to CA during both peak and submaximal exercise was similar to the decreased HR reported by Moore et al. (28) in well-acclimatized males at 4,300 m. The PV reduction observed in the present study was similar to the PV reduction observed in other males acclimatized to 4,300 m for 12 d (23). The reduction in [La] during both peak and submaximal exercise at CA compared to AA, otherwise known as the "lactate paradox," has been observed repeatedly in other investigations (3,6,35). Thus, the similarity between the physiological responses during both peak and submaximal exercise observed in our study and those observed in previous studies of well-acclimatized males at 4,300 m indicates that our volunteers were appropriately acclimatized.

Our findings demonstrate that exercise responses associated with acclimatization to 4,300 m were retained to a significant degree upon RA after 8 d at SL. Specifically, during RA,

exercise SaO_2 and $\dot{V}E{\cdot}\dot{V}CO_2^{-1}$, which generally follow the same time course and pattern as that of ventilatory acclimatization, were retained 65%-92% and 54%-86%, respectively, during the three submaximal workloads (Fig. 3). Bender et al. (4) found that increase in exercise SaO_2 and $\dot{V}E{\cdot}\dot{V}CO_2^{-1}$ were ~61% and ~92% complete after 8 d at 4,300 m. Thus, if ventilatory responses are lost at the same rate as they are acquired, exercise SaO_2 and $\dot{V}E{\cdot}\dot{V}CO_2^{-1}$ should be retained ~39% and ~8% after 8 d at SL. We were surprised by the magnitude of retention of ventilatory responses upon RA, suggesting that deacclimatization of ventilatory responses may be slower and perhaps follow a different mechanism than ventilatory responses to acclimatization. Grassi et al. (14) found that peak exercise $\dot{V}E{\cdot}\dot{V}CO_2^{-1}$ had returned completely to original SL values when measured post-exposure at SL after a 7-d deacclimatization. Thus, our retention of exercise ventilatory responses during RA is much higher than comparative responses measured at SL. This finding is reasonable given our volunteers were under hypoxic stress upon RA and hypoxia is a known stimulator of ventilation (13).

There is conflicting information concerning HR during exercise and acclimatization to altitude. Some studies suggest that HR during exercise decreases with altitude acclimatization (1,14,21), while others suggest no change (34). We found a trend for HR to decrease at all workloads from AA to CA. During exercise, HR at RA was intermediate between HR at AA and HR at CA at all workloads, suggesting a retention of some degree of cardiovascular responses to acclimatization. Asmussen and Consolazio (1) and Grassi et al. (14) reported a decrease in HR during exercise with acclimatization that was 50% and 86% complete after 1 wk at altitude. Thus, if cardiovascular responses are lost at the same rate that they are acquired, we would expect ~14%-50% retention in exercise HR response upon RA after 8 d at SL. In the

present study, HR was retained 50% at 75% $\dot{V}O_{2peak}$, indicating that perhaps acclimatization and deacclimatization for HR during exercise follow a similar time course. In support of this conclusion, Grassi et al. (14) found that the decrease in HR was retained 17% after 1 wk at low altitude, and Ferretti et al. (11) found no difference in maximal or submaximal exercise HR response measured pre- and post-exposure after 3 wk at low altitude. Thus, it appears that the decrease in HR response during exercise returns to 17%-50% of low altitude values after 1 wk at low altitude and to 100% of low altitude values after 3 wk at low altitude.

During the three submaximal exercise workloads, 55%-79% of the decrease in PV due to acclimatization was retained upon RA after 8 d at SL in the present study (Fig. 3). Krzywicki et al. (23) reported a 10% decrease in PV after 4 d at 4,300 m and a 22% decrease after 12 d at 4,300 m. Linear extrapolation from these data indicate that PV would be reduced ~16% from low altitude after 8 d at 4,300 m, which represents ~71% of the full reduction in PV. Theoretically, during deacclimatization to altitude, only 29% of the decrease in PV with acclimatization should be retained after 8 d at SL. Our values were much higher than expected, indicating again that the rate of deacclimatization, as measured by changes in PV, may follow a longer time course than the rate of acclimatization.

The pattern of the metabolic data are similar to the cardiorespiratory data in that [La] was retained between 44%-92% during the three submaximal workloads at RA in the present study (Fig. 3). Grassi et al. (14) found that 68% of the reduction in [La] was achieved after 1 wk of altitude acclimatization and that full reduction was achieved after 3 wk of high altitude acclimatization. If acclimatization and deacclimatization were to follow a similar time course, we would expect [La] to be retained ~32% after 1 wk at low altitude. Grassi et al. (14) found

that mean decrease in lactate accumulation was retained 67% after 1 wk, 40% after 2 wk, and 13% after 3 wk at low altitude. These data suggest that the deacclimatization responses for [La], like ventilation, may occur over a longer time period than acclimatization responses. The similarity in the percentage of decreased lactate response retained (~67%) after 7 d at low altitude in the study by Grassi et al. (14) and the amount of [La] retained (~75%) during RA after 8 d at SL in the present study, suggests that the added stress of hypoxia does not appear to effect the amount of [La] response retained during deacclimatization.

Although the volunteers in the present study retained a substantial portion of their altitude acclimatization as measured by their physiological responses, we did not see a significant improvement in exercise performance as measured by EXH time. The EXH time tended to increase 19% from AA to CA, but this increase was not maintained at RA. We expected some degree of the improvement in EXH time observed at CA to be maintained at RA, given the significant retention of acclimatization represented by supposedly "beneficial" physiological responses to exercise. Using EXH time as a measure of exercise performance is problematic. Psychological factors can play a prominent role in determining the point at which a volunteer reaches exhaustion. Furthermore, the measurement of EXH time is subject to large intra- and inter-subject variability which makes it difficult to show statistical significance (19).

Little is known about the rate and process of ventilatory deacclimatization to altitude. We were surprised by the magnitude of exercise ventilatory acclimatization retained upon RA. If ventilatory acclimatization is due to increased central and peripheral chemoreceptor sensitivity (5), then deacclimatization should be a reversal of this process. We previously reported, for the same group of volunteers, that resting hypoxic and hypercapnic ventilatory responsiveness

measured at SL had returned to near pre-acclimatization values by 7 d post-acclimatization, suggesting that chemosensitivity had returned to normal (29). But resting ventilation was greater 7 d post-acclimatization measured at SL than pre-acclimatization SL values (29). Since hypoxic stimulation of the carotid chemoreceptors is absent at SL, this elevated resting ventilation was likely due to the effects of decreased blood and cerebrospinal fluid (CSF) bicarbonate still present from the CA phase. Presumably, the decreased CSF bicarbonate would persist longer than the decreased blood bicarbonate given the slower time course of CSF acid-base changes (10). The probable persistence of this hypocapnic alkalosis may have set the stage for the greater exercise ventilation upon RA after 8 d at SL than when compared to exercise ventilation at AA.

Various hypotheses have been proposed to explain the reason for the reduction in [La] with exercise accompanying altitude acclimatization (16,20,27,30,35). One possible explanation for the initial and continued reduction in [La] is an increased glycogen sparing and fat oxidation during exercise with CA exposure (35). Certainly, our RER values during submaximal exercise at CA and RA suggest this as a possibility but our [GLU], [FFA], [GLY], and [COR] data neither support nor refute this as a possibility. However, recent evidence from isotopic tracer studies suggests that simple blood accumulation values often do not accurately reflect substrate uptake and release (31). Furthermore, the decreased RER values, in our study, may have been due to the combined effects of hypoxia and anorexia rather than an increase in fat utilization, since volunteers did lose BW from SL to CA. The reason for the continual expression of the "lactate paradox" upon RA after 8 d at SL may have to do with the slow reversal of hypothesized mechanisms.

Another possible reason for the retention of the "lactate paradox" during exercise is related to the retention of decreased PV (See Figure 3) during both rest and exercise upon RA after 8 d at SL. In these same test volunteers, a reduced total body water associated with altitude acclimatization was also retained ~60% measured at SL after 6 d at SL (25). Even though other studies have found no change in the oxygen delivery to the working muscle (2) during exercise in acclimatized volunteer subjects, there might be an increase in oxygen conductance from the red cell to skeletal muscle mitochondria (9). An increase in skeletal muscle oxygen conductance would limit lactate accumulation by permitting a higher rate of ATP turnover before adenylate breakdown and lactate production. Additionally, the loss of body fluid with altitude acclimatization may improve aerobic metabolism during hypoxemia due to a decrease in the oxygen diffusion distance from the red cell to skeletal muscle mitochondria (17). Since the decrease in PV was retained ~55-79% during the three submaximal workloads upon RA after 8 d at SL, there is a strong possibility that this retention may have contributed to the continued depression in [La] values at RA.

CONCLUSIONS

In summary, after an 18-d acclimatization to 4,300 m, even though submaximal exercise time to exhaustion was not improved, a large degree of exercise responses associated with acclimatization were retained upon reintroduction to altitude after eight days at sea level. The observation that these responses were retained to a greater degree than was expected by the time course of their acquisition during acclimatization, suggests that deacclimatization to altitude follows a slower time course than acclimatization. Consequently, retention of "beneficial" exercise responses associated with altitude acclimatization is likely for at least eight days in

individuals whose work, athletic competition, or recreation schedules involve intermittent sojourns to high elevations.

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The views, opinions and/or findings in this report are those of the authors, and should not be construed as an official Department of the Army position, policy or decision, unless so designated by other official documentation.

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on the use of volunteers in research.

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LIST OF FIGURES

Table 1. Peak cardiorespiratory and metabolic responses at sea level (SL), acute altitude (AA) and chronic altitude (CA).

	SL	AA	CA
$\dot{V}O_{2peak}$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	57±2	40±2*	42±3*
$[La]_{peak}$ ($mmol \cdot l^{-1}$)	9.3±0.4	7.8±1.0	4.3±0.4*†
SaO_{2peak} (%)	97±0	69±4*	73±3*
$\dot{V}E_{peak}$ ($l \cdot min^{-1}$)	157±6	166±9	184±11
HR_{peak} (bpm)	190±5	177±4*	170±5*
RER_{peak}	1.16±0.01	1.16±0.03	1.02±0.02*†

Values are means±SE; $\dot{V}O_2$, oxygen uptake; [La], blood lactate accumulation; SaO_2, arterial oxygen saturation; $\dot{V}E$, minute ventilation; HR, heart rate; RER, respiratory exchange ratio
*P<0.05 from SL
†P<0.05 from AA

Fig. 1.

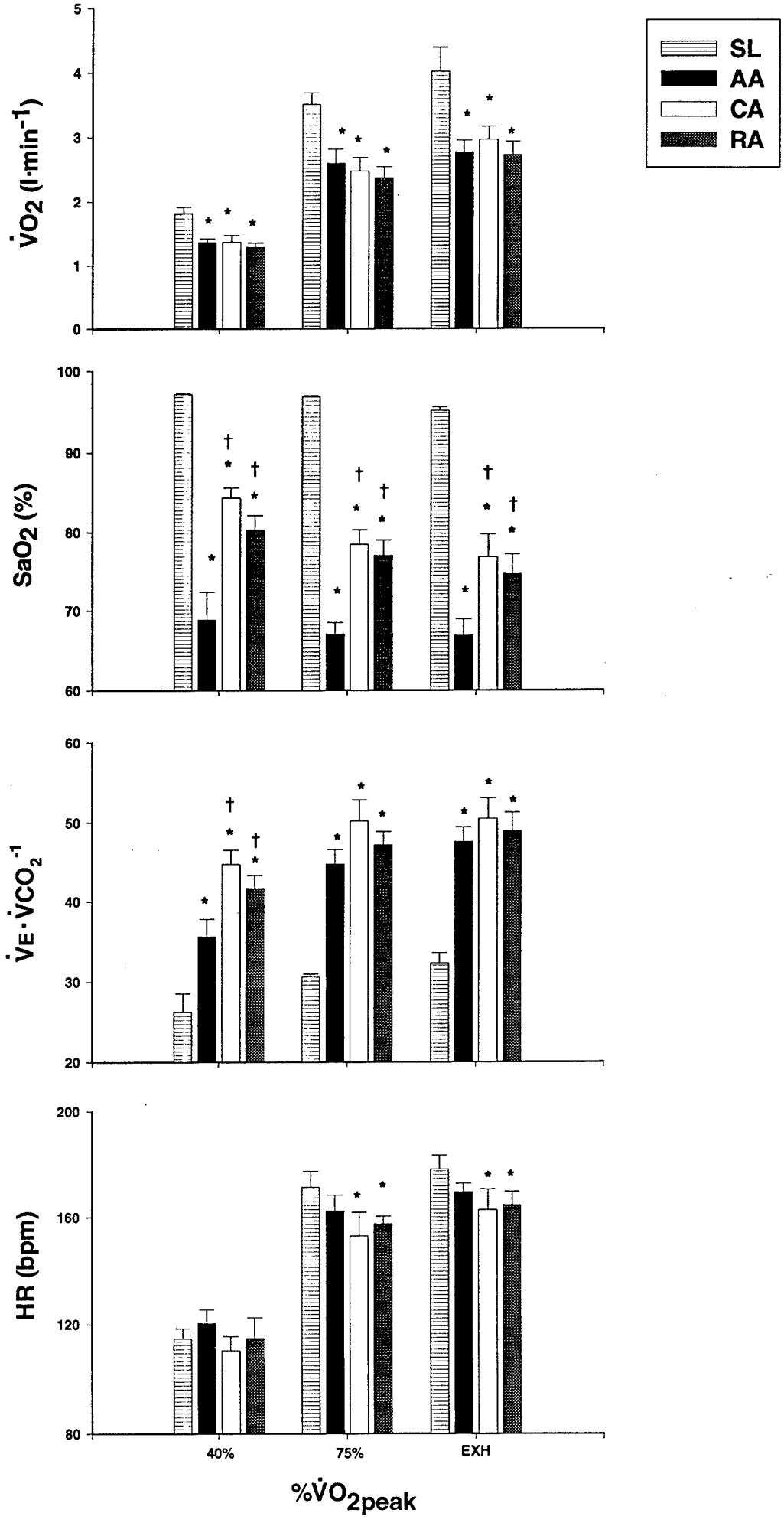

SL
AA
CA
RA
$\dot{V}O_2$ (l·min^{-1})
SaO_2 (%)
$\dot{V}_E \cdot \dot{V}CO_2^{-1}$
HR (bpm)
40%
75%
EXH
%$\dot{V}O_{2peak}$

Fig. 2

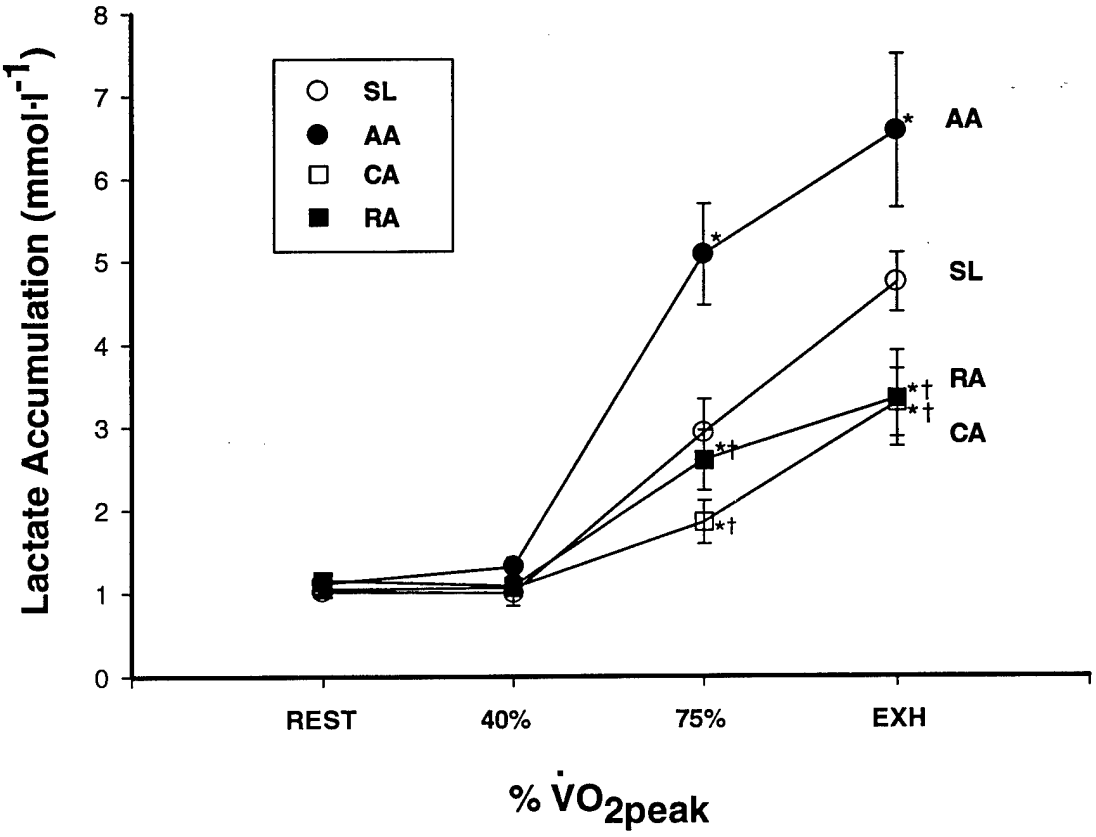
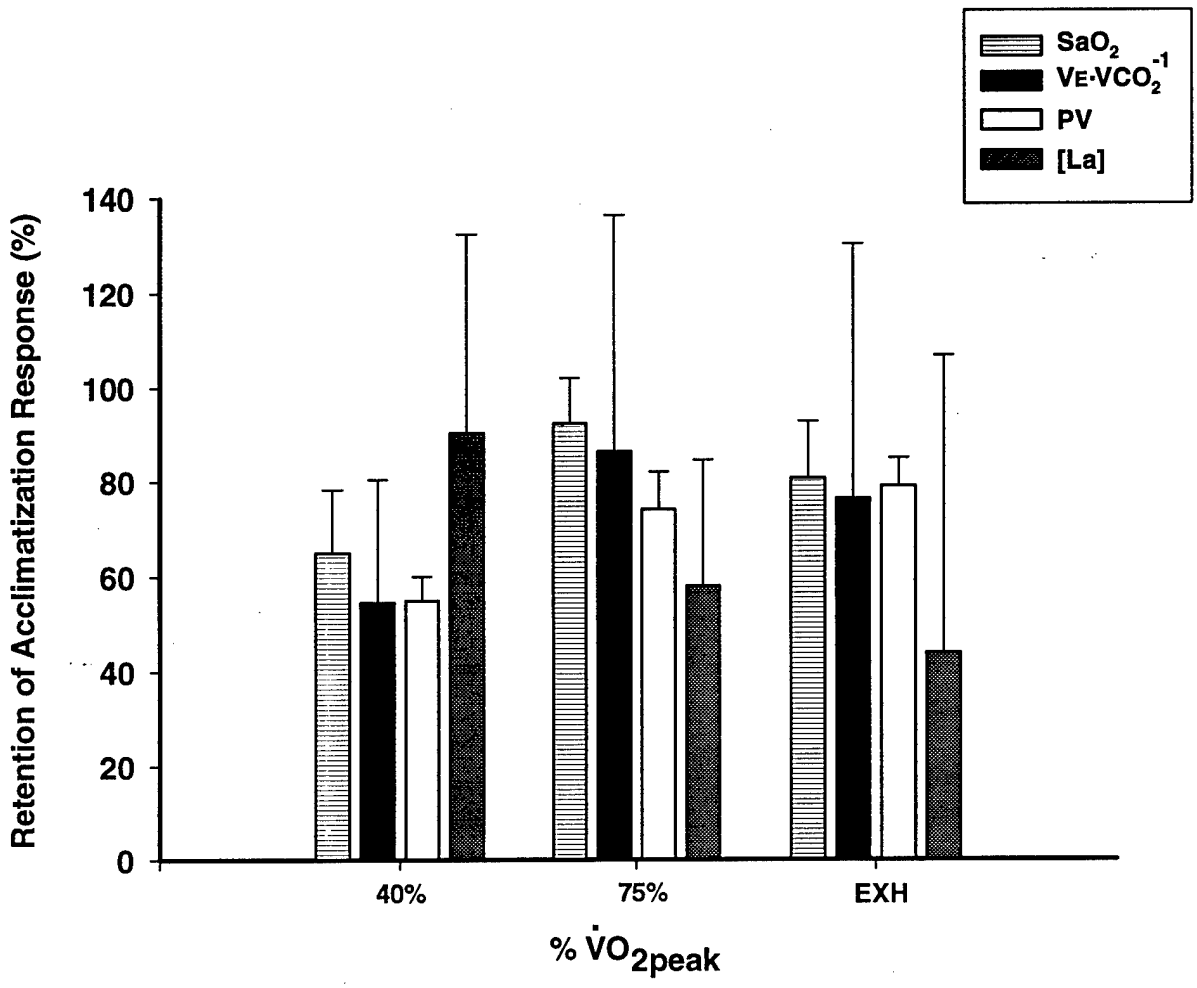

Lactate Accumulation (mmol·l-1)
8
7
6
5
4
3
2
1
0
SL
AA
CA
RA
AA
SL
RA
CA
*
*
*†
*†
*†
REST
40%
75%
EXH
% V̇O2peak

Fig. 3


SaO2
VE·VCO2-1
PV
[La]
Retention of Acclimatization Response (%)
140
120
100
80
60
40
20
0
40%
75%
EXH
% V̇O2peak